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Artistic creativity and risk for schizophrenia, bipolar disorder and unipolar depression: a Swedish population-based case-control study and sib pair analysis.

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Abstract

Background: Many studies have addressed the question of whether mental disorder is associated with creativity, but high quality epidemiological evidence has been lacking.

Aims: To test for an association between studying a creative subject in early adulthood at high school or university and later mental disorder.

Method In a case control study using linked population based registries in Sweden, N=4,454,763, we tested for associations between tertiary education in an artistic field and hospital admission with schizophrenia (N=20,333) bipolar disorder (N=28,293) or unipolar depression (N=148,365).

Results Compared to the general population, individuals with an artistic education had increased odds of developing schizophrenia (OR=1.90, 95% CI= [1.69; 2.12]) bipolar disorder (OR= 1.62 [1.50; 1.75]) and unipolar depression (OR=1.39 [1.34; 1.44]. The results remained after adjustment for IQ and other potential confounders.

Conclusions Students of artistic subjects at university are at increased risk of developing schizophrenia, bipolar disorder and unipolar depression in adulthood.

Declaration of interest: None.

[149 words]

Introduction

The notion that mental disorders are associated with enhanced creativity, intelligence or artistic talent is one of the oldest in psychiatry. Some of the most influential research in this area was based on retrospective reviews drawn from biographical sources (1) and small case control studies of people in creative professions (2). These studies have suffered from selection and information bias, combined with low statistical power. Thus, reviewing the literature in 2011, Hurlow and MacCabe concluded that there was no convincing evidence of an association and that large scale population-based studies were required (3).

Kyaga and colleagues conducted a population-based study using data from Swedish national registers, which demonstrated that people with bipolar disorder and their healthy relatives were over-represented in artistic and scientific occupations. The healthy relatives of people with schizophrenia were also over-represented in such occupations, but schizophrenia patients themselves were not, although this last finding must be interpreted cautiously owing to the low rates of employment in the schizophrenia group (4). In a separate Swedish population study, MacCabe and colleagues showed that excellent school performance at age 16 was associated with increased risk of later bipolar disorder (5), but was protective against schizophrenia and other psychoses (6), and a systematic review showed similar findings (7). This raises the question about the overlap between creativity, educational attainment and intelligence, ~~and~~ which, if any, of these markers has the strongest association with which mental disorders, ~~and~~ and to what extent they confound one another. Recently, Power *et al* have found evidence for a genetic association between creativity and

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mental disorder, showing, in the Icelandic population, that polygenetic risk scores for schizophrenia and bipolar disorder are associated with creative occupations (8). Taken together, these results lend support to the hypothesis that some aspects of intelligence and/or creativity may be associated with bipolar disorder, and possibly also schizophrenia, and that this association may be, at least partly, genetically driven.

In this study, we sought to test the hypothesis that creativity is associated with severe adult mental disorders in a national population. Our study incorporates five innovations. Firstly, we used a new proxy of creativity: studying a creative or artistic subject at university or upper secondary school. Unlike artistic occupations, artistic study predates the illness in many cases, reducing the ~~risk-probability~~ that ~~the-any~~ ~~results-association~~ might arise through reverse causation. Secondly, while some very accomplished scientific leaders could be described as creative, it is likely that many scientific graduates have a more logical or analytical cognitive style. Furthermore, most of the prior evidence of an association with mental disorder has been with artistic creativity. We therefore chose to focus on artistic, rather than scientific, creativity. Thirdly, the relationship between creativity, educational attainment and IQ is difficult to disentangle. We obtained measures of all three, to assess the extent to which they confound one another. Fourthly, we took into account shared familial factors in a sub-analysis restricted to pairs of siblings discordant for creative study. Lastly, we conducted sensitivity analyses to test the specificity of both the exposure and the outcome.

Method

Study design

The study employed a case-control design using population registers covering the whole population of Sweden. We compiled the dataset by linking data from the following registers, via the unique registration number carried by all Swedish residents.

LISA: This database holds annual registers from 1990 to 2009 and includes all individuals 16 years of age and older residing in Sweden on 1st November the previous year. This database provided demographic information including the gender and date of birth of the participants.

Higher education register: information on level and subject of study at upper secondary school and university, coded according to the Swedish educational nomenclature (SUN). SUN is a standard for classification of individual educational programs, while also allowing aggregation of programs to larger groups (9). It was created in the late 1960s, and revised in 1998-1999 (SUN 2000) to align with the International Standard Classification of Education (ISCED) 97.

Military Service Conscription Register:

Military conscription was compulsory **for men** at age 18 until 2009, although a small number of individuals were excused conscription on grounds of ill health, including learning disability. As part of their assessment, the conscripts underwent intelligence testing. The test used written questionnaires from 1969-1994 and was computer based

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thereafter. Both tests assessed four aspects of intelligence (logical/inductive, verbal, spatial/visual and theoretical/technical reasoning) and included 160 questions (40 for each dimension) (10). The results were standardised against the entire population.

Multigenerational Register: This register, which links individuals to their first-degree relatives, allowed the identification of sib pairs within the population who were registered as living in Sweden after 1960.

National Patient register. This contains details on virtually all psychiatric hospitalizations since 1973, including admission and discharge dates and the discharge diagnosis made by the treating physician. It contains outpatient contacts with specialist physicians including psychiatrists from 2001. It is coded using the International Classification of Diseases (11) version 8 (ICD-8) 1969 – 1986, 9 (ICD-9) 1987 - 1996, and ICD-10 subsequently.

Sample and caseness definitions

The sample comprised all individuals in the LISA database aged 20 to 64 on 31 December, 2009. To avoid the possibility of confounding by migration status, which is associated with both schizophrenia (12) and educational level (13), we excluded individuals who were born outside Sweden. We also excluded individuals with missing data on educational level.

Cases were defined as all individuals hospitalised with a register diagnosis of schizophrenia, bipolar disorder or unipolar depression from 1 January 1973 to 31 December 2009. These disorders were defined according to the Swedish Version of

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the International Classification of Diseases Versions 8, 9 and 10, using the following codes: Bipolar disorder: ICD-8: 296 (excluding 296.2); ICD-9: 296 (excluding 296B); ICD-10: F30-31; Schizophrenia: ICD-8 and 9: 295; ICD-10: F20; Unipolar depression: ICD-8: 296,2, 300.4; ICD-9: 296B, 300E, 311; ICD-10: F32-24 (excluding F32.3), F38-39. A hierarchical diagnostic system was used, such that if more than one diagnosis was present in any given individual, schizophrenia took precedence over bipolar disorder, which in turn took precedence over unipolar depression. For each analysis, with the exception of the sib pair analysis, the remainder of the population constituted the control group.

Definition of creative subject:

The exposure was defined as having completed a course of study in an artistically creative subject at university or *gymnasieskola* (upper secondary school).

We used two definitions of artistic creativity: a broad definition which included a wider variety of creative or artistic subjects corresponding “Art and Media” in the SUN 2000 definition, but excluding “Science and History of Art, Music, Dance, Film and Theatre”, and a narrow definition, comprising visual arts, music, dance, theatre and drama, film, radio and TV production, and fashion design. To test the specificity of the associations to particular fields of artistic ~~endeavour~~study, we defined two further sub-specialisations: visual arts, and performing arts. The university subjects corresponding to the four definitions of creative subjects are listed in Table 1.

Statistical analysis

We conducted all analyses using Stata 12.1 IC (14). For each combination of exposure and outcome, we performed logistical regression calculating odds ratios

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with 95% confidence intervals, adjusting for age and sex. In order to adjust for the possible effects of university attendance *per se*, we performed a second analysis adjusted for age, sex and highest educational level achieved. **In males only**, we performed an additional analysis adjusting for IQ at age 18 to 19. Lastly, to control for familial factors, we conducted a sibling pair analysis, comparing the odds of developing mental disorder in sibling pairs discordant for the exposure, adjusting for age, sex and highest educational level achieved.

In order to detect any unsuspected sources of bias, we conducted sensitivity analyses using a 'negative control' exposure and outcome. Negative control exposures are exposures not expected to be associated with the outcome of interest, while negative control outcomes are outcomes not expected to be associated with the exposure of interest. Substituting in the negative control variables is designed to detect confounding and bias in observational studies. The rationale underlying this ~~technique approach~~ is that, if the associations between the exposure and outcome of interest had arisen through inherent biases in the study design, undetected confounding, or other spurious mechanisms, one would expect these associations to also be present when substituting the negative ~~control~~ exposures and outcomes for the exposures and outcomes of interest (15).

We ~~therefore~~ selected a negative exposure (studying for a Law degree) and a negative outcome (diabetes, ICD-8-9: 250; ICD-10: E10-14) on the basis that they had no known or suspected aetiological associations, but had similar prevalences, to the exposures and outcomes of interest. Then, using analyses that were identical to the main analysis described above, we tested for associations between studying law and

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developing the mental ~~health~~ disorders of interest, and between studying artistically creative subjects and developing diabetes.

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Results

There were 5,462,466 individuals in the LISA database, aged 20 to 64 on 31 December 2009. Approximately 1 million of these were excluded as they were born outside Sweden, reducing the total sample to 4,474,662. A further 19,899 people were excluded as they had no data on educational level, bringing the total sample to 4,454,763.

Prevalence of exposures and outcomes:

194,039 individuals (4.36%) met the broad criterion of having studied an artistically creative subject, and 50,288 individuals (1.13%) met the narrow criteria. 50,933 individuals (1.14%) had studied the negative control subject of law and jurisprudence. Of the 194,039 who had an artistic education (broad definition), 147,477 had a sibling discordant for artistic education. The sib pair analysis therefore included 294,954 individuals.

28,293 individuals (0.64%) received a diagnosis of bipolar disorder, 20,333 individuals (0.46%) received a diagnosis of schizophrenia and 148,365 individuals (3.33%) received a diagnosis of unipolar depression. 94,363 individuals (2.12%) received diagnoses of diabetes.

Demographic characteristics of the sample

The demographic characteristics of the sample are presented in Table 2.

Association between artistically creative subject and mental disorder

Table 3 shows the associations between studying an artistically creative subject and the occurrence of mental disorders. In model I, we present the associations in the entire sample, adjusted for year of birth and sex. We found a moderate association between studying broadly defined artistic subjects and risk for bipolar disorder and unipolar depression. The association with schizophrenia was of borderline significance. The associations for all three disorders became stronger when we used the narrower definition of artistic subjects.

In model II, we additionally adjusted for highest educational level, to control for confounding by university attendance. All the associations remained, indeed the odds ratios became somewhat stronger.

In model III, we adjusted for familial factors by comparing sib pairs within families (adjusting for age sex and highest educational level). All the associations were somewhat attenuated, suggesting some confounding by familial factors.

Subtypes of artistically creative subjects

In order to test the hypotheses regarding specific associations of specific subtypes of artistic field with mental disorders, we tested for associations with visual arts and performing arts. Visual arts had consistently stronger associations with all mental health outcomes than performing arts, with odds ratios as high as three in the case of schizophrenia (Table 4).

Negative controls

Diabetes had no associations with studying and artistic subject in any of the models tested, other than the narrow definition of artistic education which showed a small protective effect against diabetes in Model I (Table 3). Law and Jurisprudence appeared protective against all three mental disorders in the crude analysis (model I) but these associations were abolished for bipolar disorder and schizophrenia after adjusting for educational level (model II), and in the sib pair analysis (model III) (Table 4), suggesting that they arose through confounding.

Models adjusted for intelligence (males only)

In males only (N=1,680,414), we were able to adjust for intelligence at age 18 from the conscript register. Adjustment for intelligence had a negligible effect on the estimates (Table 5).

Discussion

In this population-based case-control study and sibling-pair analysis, we have demonstrated an association between studying an artistically creative subject and hospitalisation for schizophrenia, bipolar disorder and unipolar depression. The associations remain when the analyses are restricted to sibling-pairs, indicating that family-level factors alone cannot explain the association.

There is some evidence for specificity to core artistic subjects, where that the association with mental illness was strongest. Furthermore, the association was strongest for core creative subjects, especially for visual arts, as compared to performing arts. It is notable that in the visual arts, most if not all practitioners are engaged in the creative process, whereas performing arts includes two categories of individual: those who create the art (composers, playwrights, choreographers), and those who perform it (musicians, actors, dancers), whose role is place more emphasis on interpretation. -more interpretive. By contrast, in the visual arts, most if not all practitioners are engaged in the creative process. Hence, the core creative subjects, particularly visual arts, may capture the concept of creativity most closely, supporting the idea that mental disorder is associated with creativity *per se*.

These findings build on those of Kyaga et al. (4). In that study, creative occupation was used as a marker of creativity. Only bipolar disorder was associated with creative occupation, with no association seen for schizophrenia or depression. The first-degree relatives of people with both bipolar disorder and schizophrenia, but not unipolar depression, were more likely to hold creative occupations. The low rates of employment for patients with schizophrenia may explain the lack of association

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between creative occupation and schizophrenia in that study. In the present study, by contrast, studying an artistic subject was associated with increased risks for all three disorders.

Limitations

Definition of exposure and comparability with previous studies

The concept of creativity is a nebulous one: in one commonly used definition, it is “the capacity to produce new or original ideas insights inventions or artistic products which are accepted by experts as being of scientific aesthetic social or technical value”(16). Capturing such a concept at the population level using routinely collected data is not straightforward. Much of the early work in this field (1, 2, 17) focused on individuals who had achieved outstanding success or esteem in their fields, or had been unusually productive. Our exposure, studying an artistic subject, may not capture the attributes of originality or external endorsement that are often seen as central to creativity. However, the decision to study a creative subject implies a disposition to creative pursuits, and it is likely that people choosing a creative subject will have higher than average levels of innate creative ability.

Other studies have used occupation as a proxy for creativity, but this has its own drawbacks. Since psychosis has a peak onset in the third decade, most patients with psychosis do not have an opportunity to establish a career, and those who do will be biased towards later onset, more transient or less severe cases. A further difficulty is that many people pursuing creative lifestyles may not hold occupations that are recognisably creative; for example, they may be listed in registers as self-employed or unemployed. We therefore argue that, while we acknowledge the limitations inherent

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in the registers, studying a creative subject has the advantage that it is likely to capture intrinsic creativity and it usually predates the onset of psychosis.

Reverse causation

Using occupation as the exposure is problematic because the career choices of people with mental disorders may be influenced by the disorder itself; for example, art or music may be used as a form of therapy, or an artistic lifestyle may be more compatible with chronic mental illness than a conventional '9 to 5' job. Given that the mean age at first hospitalisation ranged between 32 to 36 years (Table 2), and university courses are typically completed several years earlier, it is likely that scholarship in an artistic field preceded the diagnosis of mental disorder in the majority of cases, although the possibility remains that subclinical psychotic symptoms or abnormal mood states may have influenced the decision to pursue artistic studies.

Confounding

We found no evidence of confounding by age, gender, educational attainment or IQ. There was only weak evidence of confounding by family-level factors. It remains possible that other unmeasured factors are confounding the association. One possible confounder is drug misuse, which is associated with psychosis (18) and which, it has been suggested, may also be linked to creativity (19). However, in a previous study in Sweden, people in overall creative professions were shown to have reduced rates of alcohol and drug misuse (20), making this explanation unlikely.

Bias

One of the primary strengths of Swedish population-based studies is the almost total population coverage, with minimal selection bias (12). If the findings had resulted

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from any biases inherent to the study design, we would have likely seen associations with the negative exposure (Law) and the negative outcome (Diabetes), so the absence of any such associations is reassuring.

An established limitation of the sibling-comparison approach is that it increases measurement error, which generally attenuates the effect sizes (21). The fact that there is little attenuation compared to the population estimates is evidence of robust associations.

Putative explanations for the association

At the population level: Evolutionary genetics

Patients with psychosis have fewer offspring than the general population (22) (23), and that this reduced fertility is detectable at illness onset (24). The ‘balancing selection’ hypothesis holds that the genetic variants conferring risk for psychosis also carry a biological advantage, such as enhanced intelligence or creativity, and this translates into reproductive advantage in the relatives of those with psychoses, thus maintaining the frequency of risk alleles in the population (25).

However several recent findings have largely obviated the need for such explanations. Firstly, there is emerging evidence that much of the genetic susceptibility to psychosis arises through de novo or very recent mutations (26). Secondly, the common variants associated with schizophrenia are much more numerous and of smaller effect than was previously thought, with likely interactions with environmental risk factors, so the selection pressure against these variants is likely to be minimal (27). Thirdly, while schizophrenia is consistently associated with reduced fertility, this is not the

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case for affective psychoses (22, 23). A fourth consideration is that there is as yet no convincing evidence that creativity is actually associated with any reproductive advantage.

Nevertheless, a recent finding has breathed new life into the balancing selection hypothesis. Power and colleagues demonstrated that polygenic risk scores for schizophrenia and bipolar disorder were associated with membership of artistic societies or creative professions in Iceland, and replicated this finding in combined samples from the Netherlands and Sweden, indicating that the association between creativity and psychosis was likely driven by genetic factors (8).

At the individual level: Psychological explanations

Psychological theories propose that certain cognitive styles may be associated with artistic creativity and psychosis. Divergent thinking patterns, in which inventive and original links are forged between ideas, may be central to creative thinking (28, 29), but in other circumstances, give rise to thought disorder or delusion formation.

Clinical implications and future research directions

These data appear to show associations between artistic creativity and risks of severe mental illness, of comparable magnitude to several established risk factors for psychotic disorders. This may have implications for service provision, for example by raising awareness of this association in university settings, including occupational health and counselling services. It also raises the question of how arts and other creative activities might be used therapeutically. An important goal for future research will be to improve our understanding of what genetic or environmental factors might be important in launching a genetically predisposed individual on a trajectory of productive creativity rather than mental illness.

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Tables

Table 1: Classification of artistic subjects, showing wide and narrow definitions of creativity and definitions of visual and performing arts

	Course	Wide definition of artistic creativity	Narrow definition of artistic creativity	Visual Arts	Performing Arts
Arts and media, general education	Arts and media, general education	X			
Visual arts	Visual arts	X	X	X	
	Science and history of arts				
	Other courses in area	X			
Music, dance and drama	Music	X	X		X
	Dance, theatre and drama	X	X		X
	Other courses in area	X			
Media production	Media production, general education	X			
	Film, radio and TV production	X	X		
	Graphic arts technology and bookbinding	X			

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	Illustration, advertisement, graphic design and photography	X			
	Other courses in area	X			
Design	Fashion design	X	X		
	Interior design	X			
	Industrial and product design	X			
	Other courses in area	X			
Handicraft	Handicraft	X			
Arts and media, other/unspecif ied	Arts and media, other/unspecified	X			

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Table 2: Demographic characteristics of the sample

		Whole sample	Bipolar	Schizophrenia	Depression	Diabetes
N (%)		4,454,763 (100.00%)	28,293 (0.64%)	20,333 (0.46%)	148,365 (3.33%)	94,363 (2.12%)
Age on 31 December 2009 (Mean [SD])		42.31 (13.06)	44.76 (12.44)	48.68 (10.30)	42.96 (13.17)	50.96 (11.80)
Age at first hospitalisation		NA	36.48 (11.80)	32.07 (10.14)	35.91 (12.59)	40.27 (16.51)
Male (%)		2,275,400 (51.08%)	11,089 (39.19%)	12,363 (60.80%)	57,770 (38.94%)	56,384 (59.75%)
Highest educational level						
	Primary (to approx. age 16)	583,924 (13.11%)	5,236 (18.51%)	6,688 (32.89%)	29,510 (19.89%)	21,627 (22.92%)
	Secondary (To approx. age 18-19)	2,943,813 (66.08%)	18,148 (64.14%)	11,994 (58.99%)	95,347 (64.27%)	60,579 (64.20%)
	Tertiary	927,026 (20.81%)	4,909 (17.35%)	1,651 (8.12%)	23,508 (15.84%)	12,157 (12.88%)
Stanine score in cognitive assessment at age 18 (males only); mean [SD]		5.13 (1.93)	4.83 (2.00)	4.10 (2.06)	4.67 (1.98)	4.75 (1.99)

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Table 3: Odds ratios and 95% confidence intervals for associations between wide and narrow definitions of artistic education, and psychiatric disorders, with diabetes as a negative control.

	Wide definition of artistic education			Narrow definition of artistic education		
	Model I	Model II	Model III	Model I	Model II	Model III
	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
Bipolar disorder	1.29 [1.22; 1.36]	1.35 [1.27; 1.42]	1.26 [1.15; 1.39]	1.53 [1.42; 1.66]	1.62 [1.50; 1.75]	1.30 [1.13; 1.49]
Schizophrenia	1.09 [1.00; 1.19]	1.30 [1.19; 1.42]	1.19 [1.02; 1.37]	1.50 [1.34; 1.68]	1.90 [1.69; 2.12]	1.56 [1.27; 1.90]
Unipolar Depression	1.22 [1.19; 1.25]	1.29 [1.26; 1.32]	1.20 [1.15; 1.25]	1.29 [1.24; 1.34]	1.39 [1.34; 1.44]	1.21 [1.13; 1.28]
Diabetes	0.97 [0.92; 1.01]	1.04 [0.99; 1.09]	1.07 [0.99; 1.16]	0.88 [0.82; 0.95]	0.99 [0.92; 1.06]	1.09 [0.96; 1.23]

Model I: Adjusted for sex and birth year

Model II: Model I + highest achieved education level

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Model III: Within-family estimate (~~based on sibling comparisons~~ sib-pair analysis)
adjusting for unobserved familial confounders

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Table 4: Odds ratios and 95% confidence intervals for associations between subgroups of artistic education specialization (visual and performing arts), and the for the comparison exposure of Law and Jurisprudence, and psychiatric disorders

	Visual arts			Performing arts			Law and jurisprudence		
	Mod el I	Mod el II	Mod el III	Mod el I	Mod el I	Mod el III	Mod el I	Mod el II	Mod el III
	OR [95 % CI]	OR [95 % CI]	OR [95 % CI]	OR [95 % CI]	OR [95 % CI]	OR [95 % CI]	OR [95 % CI]	OR [95 % CI]	OR [95 % CI]
Bipolar disorder	1.68 [1.47; 1.92]	1.77 [1.55; 2.03]	1.41 [1.11; 1.79]	1.51 [1.37; 1.66]	1.60 [1.45; 1.76]	1.33 [1.13; 1.58]	0.78 [0.69; 0.88]	0.92 [0.81; 1.04]	0.88 [0.72; 1.08]
Schizophrenia	2.34 [1.99; 2.74]	3.00 [2.56; 3.52]	2.17 [1.58; 2.98]	1.15 [0.98; 1.35]	1.45 [1.24; 1.71]	1.30 [1.00; 1.70]	0.48 [0.39; 0.58]	0.93 [0.76; 1.14]	0.77 [0.57; 1.03]
Depression	1.38 [1.29; 1.47]	1.49 [1.40; 1.58]	1.21 [1.08; 1.34]	1.25 [1.20; 1.31]	1.35 [1.30; 1.42]	1.19 [1.11; 1.29]	0.73 [0.69; 0.77]	0.93 [0.88; 0.98]	0.95 [0.87; 1.04]

Model I: Adjusted for sex and birth year

Model II: Model I + highest achieved education level

Model III: Within-family estimate (based on sibling comparison sib-pair analysis) adjusting for unobserved familial confounders

Table 5: **In males only;** Odds ratios and 95% confidence intervals for associations between wide and narrow definitions of artistic education, and psychiatric disorders, with additional adjustment for intelligence

	Wide definition of artistic education				Narrow definition of artistic education			
	Model I	Model II	Model III	Model IV	Model I	Model II	Model III	Model IV
	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
Bipolar disorder	1.53 [1.35; 1.73]	1.58 [1.39; 1.79]	1.59 [1.40; 1.80]	1.39 [1.03; 1.88]	1.92 [1.61; 2.29]	2.01 [1.69; 2.40]	2.01 [1.69; 2.40]	2.12 [1.32; 3.41]
Schizophrenia	1.35 [1.17; 1.55]	1.60 [1.39; 1.84]	1.66 [1.44; 1.91]	1.38 [0.97; 1.98]	1.70 [1.40; 2.06]	2.19 [1.80; 2.65]	2.24 [1.84; 2.72]	1.72 [1.06; 2.79]
Depression	1.32 [1.25; 1.40]	1.43 [1.36; 1.52]	1.45 [1.37; 1.54]	1.14 [1.00; 1.31]	1.41 [1.30; 1.54]	1.59 [1.46; 1.73]	1.60 [1.47; 1.74]	1.24 [1.01; 1.53]

Model I: Adjusted for birth year

Model II: Model I + highest achieved education level

Model III: Model II + intelligence tests at 18

Model IV: Within-family estimate (based on sibling comparisons sib-pair analysis)

adjusting for unobserved familial confounders

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